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An Unusual Reaction of Cyclic Enol Ethers with Titanium(III) Tetrahydroborate

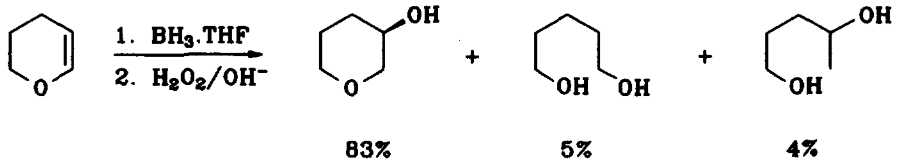
K.S. Ravikumar[a,b] and Srinivasan Chandrasekaran*[,a]

a. Department of Organic Chemistry, Indian Institute of Science, Bangalore-560 012, India.
b. IDL-Nitro Nobel Basic Research Institute, Sankey Road, Malleswaram, Bangalore-560 003, India.

Abstract: Titanium(III) Tetrahydroborate formed *in situ* from titanium tetrachloride and benzyltriethylammonium tetrahydroborate (1:4) readily reacts with cyclic enol ethers in dichloromethane at -20°C to give the corresponding acyclic diols in high yields after simple aqueous work-up. © 1997 Elsevier Science Ltd. All rights reserved.

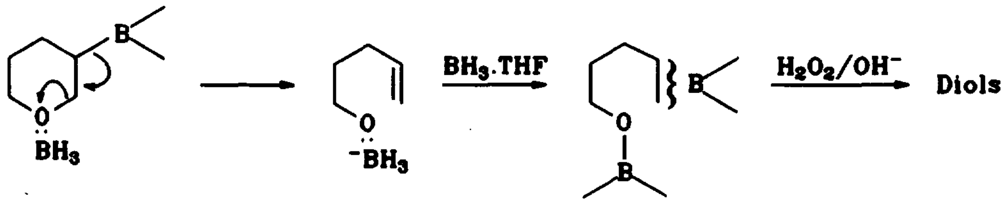
Hydroboration of heterocycles containing a carbon-carbon double bond adjacent to the hetero atom is highly regioselective. The heteroatom directs the addition of borane exclusively to the β-position to give β-organo boranes which on oxidation affords the corresponding β-hydroxy heterocycles (**Scheme 1**).[1]

Scheme 1



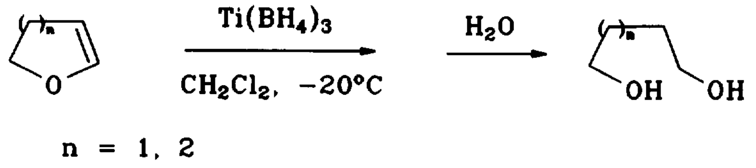
Excess hydride and prolonged reaction time can cause the cleavage of the intermediate trialkylborane to yield initially unsaturated products, which then undergo further hydroboration to afford the diols (**Scheme 2**).[2]

Scheme 2



Recently, we reported an unusual *anti*-Markovnikov hydration of alkenes[3] with titanium(III) tetrahydroborate, $Ti(BH_4)_3$, 1 without involving a formal oxidative work-up.[4] In order to explore the scope and utility of this reagent, we studied the reactivity of 1 with α,β-unsaturated carbonyl compounds, and found that this transition metal borohydride produces the corresponding allylic alcohols in about 90% selectivity.[5] Since, the reagent system behaves differently from diborane, we believed it would be of interest to study the reactivity of electron rich enol ether double bonds with this reagent system.

We now report that $Ti(BH_4)_3$, 1 derived from $TiCl_4$ and benzyltriethylammonium tetrahydroborate[6] (1:4) effects a facile and smooth conversion of cyclic enol ethers in CH_2Cl_2 (-20°C, 6-8 h) to the corresponding acyclic diols exclusively in excellent yields. The results of this remarkably unusual reaction are summarized in **Table 1**. When dihydrofuran, 2 and dihydropyran, 4 were allowed to react with tetrahydroborate, 1 butan-1,4-diol, 3 and pentan-1,5-diol, 5 respectively were formed. Substituted cyclic enol ether 6 on similar reaction gave diol 7 exclusively. 5,6-Indenyldihydro-2(H)-pyran, 8 and *cis*-oxa-1,$\Delta_{2,3}$-octalin, 10 on treatment with 1 afforded the corresponding diols 9 and 11, respectively in good yields.



(eq.1)

Interestingly, the reaction of 1 with 1-methoxycyclohexene, 12 and silylenol ether, 14 were analogous to the normal hydroboration-oxidation leading to the formation of *trans*-2-methoxycyclohexanol, 13 and *trans*-1,2-cyclohexanediol, 15 respectively.

When dihydropyran, 4 was treated with benzyltriethylammonium tetrahydroborate, the starting material was recovered unchanged. In the absence of benzyltriethylammonium tetrahydroborate, the dihydropyran, 4 got polymerized on treatment with $TiCl_4$ (**Scheme 3**). A blank reaction has also been done

Scheme 3

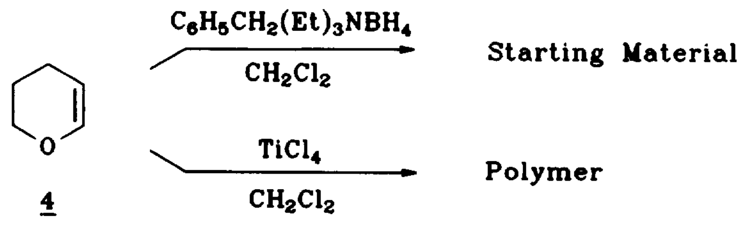
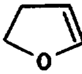
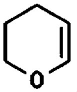
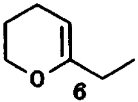
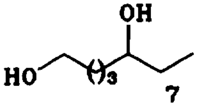
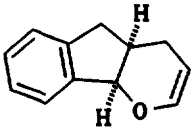
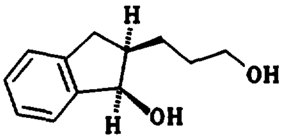
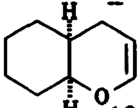
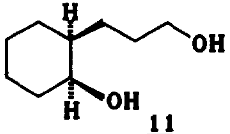
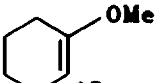
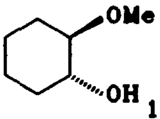
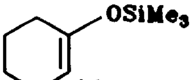
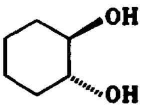
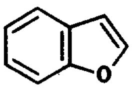


Table 1

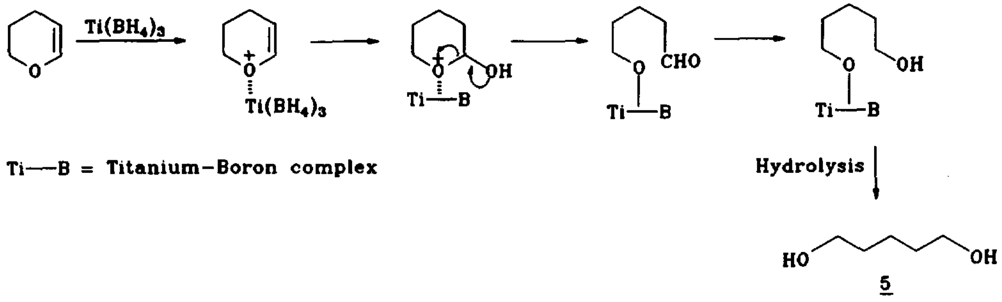
Entry	Substrate	Time (h)	Product	Yield (%)
1.	 2	6	 3	89
2.	 4	6	 5	87
3.	 6	8	 7	61
4.	 8	6	 9	73
5.	 10	6	 11	71
6.	 12	2	 13	80
7.	 14	1	 15	90
8.	 16	3	Complex Mixture	-

to rule out the possibility of a simple hydrolysis of the enol ether followed by reduction to give the product.

The mechanism of Ti(BH$_4$)$_3$ reaction with enol ether is not clear. Based on the experimental observations it appears that simple diborane is not involved in this transformation and Ti^{+3} probably plays a major role in this reaction.[7]

A plausible mechanism has been proposed for this unusual reaction in **Scheme 4**. The nonbonded pair of electrons on oxygen complex with Ti(III) reagent and the hydration occurs at the carbon bearing the oxygen followed by reduction to yield the diol.

Scheme 4



Ti—B = Titanium–Boron complex

EXPERIMENTAL SECTION

General Remarks. ^1H NMR spectra were recorded at 90 MHz in $CDCl_3$. TLC were performed on 0.25 mm E.Merck precoated silica plates (60F-254). All the products were purified by flash column chromatography on silica gel. The melting points reported are uncorrected. Dihydrofuran and dihydropyran were purchased from Aldrich and distilled freshly before use. All other cyclic enol ethers were prepared according to the literature procedures.[8] A stock solution of titanium tetrachloride in dry dichloromethane (9.5% w/v) was used.

General Procedure for the Preparation of Titanium(III) Tetrahydroborate, $Ti(BH_4)_3$. 1 (4 mmol).

To a stirred stock solution of $TiCl_4$ (4 mL, 4 mmol), benzyltriethylammonium borohydride (3.31 g, 16 mmol) in dry CH_2Cl_2 (15 mL), was slowly added under N_2 at -20°C and the reaction mixture was stirred for 0.5h and gaseous by products were removed under a positive pressure of dry N_2.

General Procedure for the Reaction of enol ethers with $Ti(BH_4)_3$, 1.

The dihydrofuran 2 (0.28 g, 4 mmol) in dry CH_2Cl_2 (2 mL) was added into a solution of tetrahydroborate 1 (4 mmol) and it was stirred for 6 h (-20°C). A solution of saturated aqueous K_2CO_3 (5 mL) was added and stirred for an additional 15 min (25°C). The reaction mixture was extracted with EtOAc (3x25 mL) and dried (Na_2SO_4). Removal of solvent followed by bulb-to-bulb distillation under vacuum afforded 1,4-butane diol, 3 as a colorless viscous liquid (0.32 g, 89%); bp: 78-80°C/2 mm (lit.,[9] 127°C/20 mm); IR (neat): ν 3360 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.6-1.8 (m, 4H), 2.65-3.25 (br, 2H, exchangeable, OH), 3.45-3.85 (t, 4H).

***1,5-Pentanediol,* 5**.[10] Yield: 0.362 g, 87%; bp: 84-87°C/2 mm (lit.,[10] 118-120°C/8 mm); IR (neat): ν 3316 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.4-1.8 (br, m, 6H), 1.8-2.0 (br, 2H, exchangeable, OH), 3.45-3.9 (t, 4H).

***1,5-Heptanediol,* 7**.[11] Yield: 0.323 g, 61%; IR (thin film): ν 3349 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.5-1.0 (t, 3H), 1.0-2.0 (complex m, 8H), 2.1-2.7 (br, 2H, exchangeable OH), 3.25-3.75 (m, 3H).

***cis-2-(3-Hydroxypropyl)-indan-1-ol,* 9**.[12] Yield: 0.561 g, 73%; IR (thin film): ν 3560, 3020, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.5-2.0 (m, 6H), 2.1-2.5 (m, 1H), 2.6-3.0 (m, 2H), 3.6-3.8 (m, 2H), 4.9-5.1 (d, 1H), 7.25 (br, s, 4H); Analysis Found: $C_{12}H_{16}O_2$ C, 74.64% ; H, 8.33% (Calcd. C, 74.97%; H, 8.39%).

***cis-2-(3-Hydroxypropyl)cyclohexanol,* 11**.[13] Yield: 0.448 g, 71%; IR (thin film): ν 3360 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.1-2.0 (m, 15H), 3.6-3.8 (m, 1H), 3.90 (m, 1H).

***trans-2-methoxycyclohexanol,* 13**.[14] Yield: 0.418 g, 80%; IR (neat): 3360 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.0-2.4 (br m, 10H), 2.8-3.0 (br, 1H, OH), 3.3 (s, 3H, OCH_3); MS(m/z): 130 (M^+), 112, 98, 84, 71, 58.

***trans-Cyclohexane-1,2-diol,* 15**.[14] Yield: 0.419 g, 90%; mp: 100-102°C (lit.,[15] mp 105°C); IR (thin film): ν 3380, 2945, 2870, 1080, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.0-2.2 (m, 8H), 3.33 (m, 2H), 2.4-3.0 (s, 2H, OH).

Reaction of benzofuran, 16 with 1.

The compound, **16** (0.236 g, 2 mmol) was added into the solution **1** (2 mmol) and allowed to react for 3h as described earlier. After the usual work-up, the product obtained was found to be a complex mixture.

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